PATENT
Docket No.: **19603/448 (CRF D-1593C)**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Barany et al.	Examiner: K. Horlick
Serial No.	:	09/918,156	
Cnfrm. No.	:	4406	Art Unit: 1637
Filed	:	July 30, 2001	
For	:	DETECTION OF NUCLEIC ACID SEQUENCE DIFFERENCES USING COUPLED LIGASE DETECTION AND POLYMERASE CHAIN REACTIONS	

DECLARATION OF FRANCIS BARANY, MATTHEW LUBIN, GEORGE BARANY, AND ROBERT P. HAMMER UNDER 37 CFR § 1.131

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, Francis Barany, Matthew Lubin, George Barany, and Robert P. Hammer, pursuant to 37 CFR § 1.131 declare that:

1. We are the inventors of the above-identified patent application.

2. Prior to June 22, 1994, we conceived and diligently reduced to practice, in the United States, the invention claimed in the above-identified patent application. Evidence of this conception prior to June 22, 1994, is provided in attached Exhibit 1. For purposes of this declaration, the dates (and unrelated subject matter) have been removed from Exhibit 1, as indicated by the REDACTED stamp.

3. Exhibit 1 is a true copy of pages from Francis Barany, Ph.D.'s grant proposal to the Department of Health and Human Services, prepared prior to June 22, 1994, which discloses the development of a multiplex ligase detection reaction/polymerase chain reaction (LDR/PCR) system. (See Exhibit 1 at page 2 of

6). Exhibit 1 also teaches the design of LDR primers for the detection of tumor genes; all of these primers have common artificial PCR primer sequences to allow subsequent amplification using only two PCR primers (Exhibit 1 at page 4 of 6 (Fig. 16)). This LDR/PCR system is illustrated in Figure 15 of Exhibit 1 (Exhibit 1 at page 3 of 6). In particular, Figure 15 illustrates the quantification of gene amplifications and deletions using LDR/PCR as follows. A sample containing a plurality of DNA templates is denatured at 94°C. The LDR primers are added, allowed to anneal to complementary sequences on the DNA templates, and ligated with a thermostable ligase. A DNA polymerase is added and PCR is carried out to amplify all LDR products simultaneously using two common "zip code" primers. As shown in Figure 15, the zip code primers are labeled to allow for detection of the extension products following PCR. Detection is carried out either by separation and quantification of different sized labeled ligation products or by capture on the appropriate oligonucleotide or PNA addressable array (Exhibit 1 at page 5 of 6 (1st full para.)).

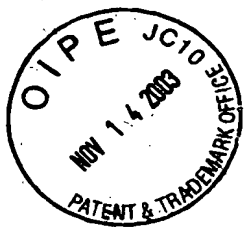
4. We hereby declare that all statements made herein of our own knowledge are true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that any such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Nov 7, 2003 — Dr. Francis Barany
Francis Barany

_____, 2003 — _____
Matthew Lubin

_____, 2003 — _____
George Barany

_____, 2003 — _____
Robert P. Hammer



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_____, 2003 _____
Francis Barany

Nov 6, 2003 Matthew B. Lubin
Matthew Lubin

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George Barany

_____, 2003 _____
Robert P. Hammer

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November 6, 2003 George Barany
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Francis Barany

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Matthew Lubin

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George Barany

Novem. 6th, 2003 
Robert P. Hammer